REMARKS

In response to the Office Action of February 16, 2006, claim 28 is hereby amended. Claims 28-39 were rejected under 35 U.S.C. § 103(a). Each of the specific rejections is addressed below.

Rejections under 35 U.S.C. § 103(a)

The Examiner bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103. In determining obviousness, one must focus on Applicant's invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 USPQ2d 1241,1246 (Fed. Cir. 1991). The primary inquiry is:

> whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success . . . Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure.

In re Dow Chemical, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). To establish obviousness, both the elements of the claimed invention plus the motivation to combine the elements must be present in the prior art. *Ex parte Hiyamizu*, 10 USPQ2d 1393, 1394 (PTO Bd. App. Intf., 1988). Thus, if an element recited in the claims is not described in the cited prior art references, then *prima facie* obviousness is not established.

The Examiner has rejected claims 28 and 32-35 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* (1992) Nature 355:850-852 in view of Hilvert *et al.* (U.S. Pat. No. 5,208,152) (the '152 patent). Regarding independent claim 28, the Examiner asserts that Ellington *et al.* teach a method of obtaining single-stranded DNA molecules capable of ligand binding that are isolated via selection and amplification *in vitro*. In addition, Ellington *et al.* teach that nucleic acid aptamers may be new catalysts for chemical transformations that are analogous to catalytic antibodies. The Examiner asserts that the '152 patent teaches the use of a catalytic antibody to perform a Diels-Alder reaction. The Examiner further asserts that this reference teaches that it would be beneficial to find a specific catalyst for Diels-Alder reactions. From these references, the Examiner concludes that it would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the ligand binding nucleic acid apatmers of Ellington *et al.* to couple with a first reactant and catalyze the

Diels-Alder reaction with a free reactant to produce a cyclohexene derivative product library. Regarding dependent claims 32-35, the Examiner asserts that Ellington *et al.* teach the use of DNA oligomers having conserved and random sequences (claim 32), the use of single stranded DNA (claim 33), and that different single stranded-DNA oligomers can be selected to fold into specific binding structures (claims 34 and 35).

In response to this rejection claim 28 has been amended to clarify that the product library is produced by contacting the mixture of first reactants with a mixture of different free reactants to produce a product library comprised of a mixture of products. Support for this amendment can be found on page 8, line 12 and page 13, lines 12-17 of the Specification. For the reasons discussed below, Applicant maintains that independent claim 28 and dependent claims 29-39 are not rendered obvious by the references relied on by the Examiner.

As discussed in Applicant's previous response, the Ellington *et al.* reference teaches a method for selecting nucleic acid ligands that bind specifically to a target from a pool of random sequences. The method taught by Ellington *et al.* for selecting these nucleic acid ligands is comprised of the steps of: preparing a pool of random DNA sequences, selecting the DNA sequences that bind to the target and amplifying these sequences *in vitro*. (Abstract, lines 1-4). As noted by the Examiner, the method is demonstrated by application to three different targets: cibacron blue (CB), reactive green 19 (GR) and reactive blue 4 (B4). As delineated in the reference, however, each of the three selections was independently performed on three separate columns (page 850, col. 2, 1st full paragraph and page 851, col. 1, paragraph following Table 1) to produce three separate mixtures of nucleic acids. Thus, to the extent that there is even a product library in Ellington *et al.*, that library is comprised solely of nucleic acids that bind to a specific target. The only diversity in such library is in the sequences of the nucleic acid ligands.

As also provided in Applicant's prior response, the Ellington *et al.* reference suggests that the nucleic acid ligands selected may be able to serve as a catalyst for a subsequent reaction. (page 852, col. 2, last paragraph). The reference provides no actual examples of the use of DNA ligands as catalysts for any reaction. Nor does the reference provide any suggestion or guidance as to the types of reactions that may be catalyzed by the selected ligands. Further, there is no suggestion in the reference of combining the nucleic acid catalysts with different reactants to form a product library comprised of different products.

The '152 patent, as noted by the Examiner, teaches the use of a catalytic antibody to perform a single type of Diels-Alder reaction. As in the case of the Ellington *et al.* reference, the '152 patent does not teach or suggest the combination of a mixture of different reactants and catalysts to form a product comprised of a mixture of different Diels-Alder products.

By contrast, the instant application as set forth in claim 28, as amended, is directed toward a method for forming a cyclohexene derivatized product library comprised of a mixture of different products. The product library is formed by the reaction of a mixture of first reactants each coupled to a nucleic acid ligand with a mixture of different free reactants. The first reactant may be either a diene or a dienophile. The reaction is facilitated by the nucleic acid ligands that are coupled to the first reactants. Thus, each library member is attached to the nucleic acid that facilitated its formation.

Applicant maintains that the Ellington *et al.* reference in no way teaches or suggests the Applicant's claimed method of producing a cyclohexene derivatized product library, comprised of a mixture of different products. Rather, as noted above, Ellington *et al.* teach a method for selecting nucleic acid ligands that bind to a specific target and suggests that these ligands may be able to serve as a catalyst for a subsequent reaction. Thus, at the most Ellington *et al.* suggest that it might be obvious to try to use their method to identify a catalyst to some unidentified reaction. Ellington *et al.* merely provide that "DNA like RNA may be able to catalyse chemical transformations." (page 852, col. 2, last paragraph). Likewise, the '152 patent does not teach or suggest the method of the instant invention. This reference merely teaches an antibody capable of catalyzing one specific type of Diels-Alder. As noted above, if an element recited in the claims is not described in the cited prior art references, then *prima facie* obviousness is not established. For this reason, Applicants do not believe that the cited references, either alone or in combination, render the method of the instant invention as set forth in independent claim 28, as amended, and dependent claims 32-35 obvious. Reconsideration is respectfully requested.

The Examiner has rejected claim 29 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* in view of Hilvert *et al.* as applied to claim 28 above and further in view of Woo *et al.* (1991) J. Amer Chem. 113:55457-5459. Claim 29 of the instant invention is drawn to the method of claim 28 further comprising a linker group between the first reactant and the nucleic acid. The Examiner reasons that while neither Ellington *et al.* nor the '152 patent teach the use

of linkers, Woo *et al.* teach the use of psoralen probes that are tethered to oligonucleotides. As discussed in detail above, the Ellington *et al.* reference, taken either alone or in combination with the '152 patent, does not teach or suggest the method of this invention. Woo *et al.* is merely cited as teaching linkers and therefore does not cure this defect. Reconsideration is respectfully requested.

The Examiner has rejected claims 30 and 31 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* in view of Hilvert *et al.* and Woo *et al.* as applied to claim 29 above and further in view of Cload *et al.* (1993) J. Am. Chem. Soc 115:5005-5014 as defined by Jolly (1984) Modern Inorganic Chemistry, McGraw Hill. Claim 30 of the instant invention is drawn to the method of claim 29 wherein the linker has a size in the range of 10 to 1000 Å and claim 31 is drawn to the method of claim 30 wherein said linker is selected from PEG, polyvinyl alcohol, polyacrylates and polypeptides. The Examiner reasons that Cload *et al.* teach the use of oligonucleotide probes tethered to a PEG linker (claim 31) and the combination of Jolly and Cload *et al.* clearly establish the length of the linker taught by Cload *et al.* as being between 10 and 1000 Å (claim 30). As discussed in detail above, the Ellington *et al.* reference taken either alone or in combination with the '152 patent and Woo *et al.* does not teach or suggest the method of this invention and thus does not render it obvious. The Cload *et al.* and Jolly references do not cure this defect and thus do not render dependent claims 30 and 31 obvious. Reconsideration is respectfully requested.

The Examiner has rejected claims 36-39 under 35 U.S.C. § 103(a) as being unpatentable over Ellington *et al.* in view of Hilvert *et al.* and further in view of Verdine (PCT International Publication No. WO 93/ 14108). Claim 36 of the instant invention is drawn to the method of claim 28 wherein nucleic acid test mixture comprises nucleic acids having one or more functional groups as set forth in the claim. Claims 37 to 39 are drawn to the method of claim 36 wherein the functional group is positioned at the ribose ring (claim 37), the base (claim 38) or the phosphate group (claim 39). Verdine is cited as teaching the attachment of functional groups at various positions of nucleic acids including the ribose position, the base of the nucleic acid and the phosphate group. As discussed in detail above, the Ellington *et al.* reference taken either alone or in combination with the '152 patent does not teach or suggest the method of this

invention. The Verdine reference does not cure this defect and thus does not render dependent claims 36-39 obvious. Reconsideration is respectfully requested.

Applicant believes that the pending claims are now in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117 if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

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